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One or two doses of oral cholera vaccine: What are the options?



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A child in Artibonite Valley region of Haiti receives oral cholera vaccine. Photo: Jon Lascher, Courtesy of Partners In Health (2012).

How can we do the most good with the limited resources available? Or, in the case of cholera vaccination, how can we avert the largest number of cholera cases given a shortage in vaccine and resources to deliver it?

It is well-known that killed, whole-cell, oral cholera vaccine protects against cholera. A series of carefully planned and well executed efficacy and effectiveness trials in Bangladesh, India, Peru, Mozambique, Zanzibar, Guinea, and Haiti have demonstrated this (1-8).

Most of these trials used two doses of vaccine, administered two weeks apart. The rationale for using two-doses with an interval of two weeks was to define a vaccination strategy most likely to be successful and that could be quickly implemented during an outbreak. When the trials were planned, it seemed unlikely that a single vaccine dose would be sufficiently efficacious. A shorter interval between doses — for example one week — might not prime the immune system in time for the second dose to deliver a booster response. Based on the evidence generated by these successful trials, the two-dose, two-week method became considered the standard way to use oral cholera vaccine.

However, since these original clinical trials were conducted, new evidence suggests that the standard method for immunizing may need to be reconsidered. Is it possible that a different dosing interval might be better, or that a single dose might be similarly effective and thus more cost effective than the standard two-dose, two-week plan? When considering this question, recall that effectiveness is not the same as efficacy (reduction in rates of disease). One way to consider effectiveness is to determine the **number of cases (or deaths) averted per 1,000 doses of vaccine delivered** and cost-effectiveness is measured by **dollars per case (or death) averted**.

Although two doses of vaccine do provide a higher level of efficacy than a single dose, recent data indicate that a single dose does provide some protection. This finding is important for two reasons.

First, if a two-dose strategy is used, one can assume that protection starts soon after the first dose—probably within a week—and this allows for more flexibility in the timing of the second dose. Many vaccination campaigns find that it would be logistically more feasible to use a longer time interval in between doses.

Second, it is reasonable to assume that if the first dose has an efficacy of at least 50% of that for two doses, a single-dose strategy would avert the same number of cholera cases when a single dose is given to twice as many people. If the single-dose efficacy was greater than 50% (relative to two doses), the single dose would actually prevent **more** cases when given to twice as many people. In a new [paper](#) [3] published by members of the DOVE project in PLoS Medicine, a more in-depth analysis shows that even a much weaker single dose may be preferable to two doses when vaccine is limited (9).

Why would anyone organize a vaccine campaign that is considered less efficacious than the “standard” two-dose campaign? Would this be considered ethical? This kind of problem is unfortunately all too common in global health.

To illustrate, if 100,000 doses were allocated to immunize an internally displaced persons camp with a population of 100,000, would it be better to give a single dose to everyone, or to give two doses to half of the people in the camp? If two doses provide 70% protection and a single dose provides 40% protection, the single dose given to all 100,000 persons in the camp will avert more cases than the two-dose campaign when only half, or 50,000 persons, receive the vaccine. In addition to this fairly simple calculation of effectiveness, the single-dose campaign will be logistically easier and more cost-effective to carry out, and the campaign could be completed more quickly. By completing the campaign quickly, the single-dose strategy could even head off a cholera outbreak that was just beginning.

An alternative to the single-dose campaign is the “modified” two-dose campaign, in which a single dose is given to the population, and a second dose is given at a later time when more vaccine becomes available. This strategy has not been validated, but clearly, considerations for applying oral cholera vaccine should go beyond the standard two-dose, two-week strategy. Alternative strategies should be considered to understand other effective ways to use oral cholera vaccine to avert cholera cases and deaths.

For more information on the one-dose versus two-dose regimen, please read a recent publication by Andrew Azman and others of the DOVE project: “[The Impact of a One-Dose versus Two-Dose Oral Cholera Vaccine Regimen in Outbreak Settings: A Modeling Study](#) [3],” published in PLoS Medicine.

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[3] <http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001867>